FIG. 1

```
LOCUS       HSTGFB3M     2574 bp    RNA            PRI       12-SEP-1993
DEFINITION  Human mRNA for transforming growth factor-beta 3 (TGF-beta
            3).
ACCESSION   X14149
NID         g37095
KEYWORDS    growth factor; transforming growth factor; transforming
            growth factor-beta 3.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae;
            Homo.
REFERENCE   1 (bases 1 to 2574)
  AUTHORS   Chen,E.Y.
  TITLE     Direct Submission
  JOURNAL   Submitted (23-MAR-1989) Chen E.Y., Genentech Inc., 460 Pt.
            San Bruno Blvd., San Francisco, CA 94080, USA
REFERENCE   2  (bases 1 to 2574)
  AUTHORS   Derynck,R., Lindquist,P.B., Lee,A., Wen,D., Tamm,J.,
            Graycar,J.L., Rhee,L., Mason,A.J., Miller,D.A.,
            Coffey,R.J., Moses,H.L. and Chen,E.Y.
  TITLE     A new type of transforming growth factor-beta, TGF-beta 3
  JOURNAL   EMBO J. 7 (12), 3737-3743 (1988)
  MEDLINE   89091120
COMMENT     See <J03241> for alternative sequence of TGF-beta 3.
FEATURES             Location/Qualifiers
     source          1..2574
                     /organism="Homo sapiens"
                          /db_xref="taxon:9606"
                          /tissue_type="placenta, ovary glioblastoma"
                          /cell_line="A172 glioblastoma"
                          /chromosome="14q24"
     CDS             254..1492
                          /note="TGF-beta 3 (AA 1-412)"
                          /codon_start=1
                          /db_xref="PID:g37096"
                          /db_xref="SWISS-PROT:P10600"
                     /translation="MKMHLQRALVVLALLNFATVSLSLSTCTTLDFGHIKKKRVEAIR
                     GQILSKLRLTSPPEPTVMTHVPYQVLALYNSTRELLEEMHGEREEGCTQENTESEYYA
                     KEIHKFDMIQGLAEHNELAVCPKGITSKVFRFNVSSVEKNRTNLFRAEFRVLRVPNPS
                     SKRNEQRIELFQILRPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTVREWLLRRESN
                     LGLEISIHCPCHTFQPNGDILENIHEVMEIKFKGVDNEDDHGRGDLGRLKKQKDHHNP
                     HLILMMIPPHRLDNPGQGGQRKKRALDTNYCFRNLEENCCVRPLYIDFRQDLGWKWVH
                     EPKGYYANFCSGPCPYLRSADTTHSTVLGLYNTLNPEASASPCCVPQDLEPLTILYYV
                     GRTPKVEQLSNMVVKSCKCS"
BASE COUNT       629 a    680 c    666 g    599 t
```

FIG. 1 (cont'd)


```
ORIGIN
        1 cctgtttaga cacatggaca acaatcccag cgctacaagg cacacagtcc gcttcttcgt
       61 cctcagggtt gccagcgctt cctggaagtc ctgaagctct cgcagtgcag tgagttcatg
      121 caccttcttg ccaagcctca gtctttggga tctggggagg ccgcctggtt ttcctccctc
      181 cttctgcacg tctgctgggg tctcttcctc tccaggcctt gccgtccccc tggcctctct
      241 tcccagctca cacatgaaga tgcacttgca aagggctctg gtggtcctgg ccctgctgaa
      301 ctttgccacg gtcagcctct ctctgtccac ttgcaccacc ttggacttcg gccacatcaa
      361 gaagaagagg gtggaagcca ttaggggaca gatcttgagc aagctcaggc tcaccagccc
      421 ccctgagcca acggtgatga cccacgtccc ctatcaggtc ctggcccttt acaacagcac
      481 ccgggagctg ctggaggaga tgcatgggga gagggaggaa ggctgcaccc aggaaaacac
      541 cgagtcggaa tactatgcca aagaaatcca taaattcgac atgatccagg ggctggcgga
      601 gcacaacgaa ctggctgtct gccctaaagg aattacctcc aaggttttcc gcttcaatgt
      661 gtcctcagtg gagaaaaata gaaccaacct attccgagca gaattccggg tcttgcgggt
      721 gcccaacccc agctctaagc ggaatgagca gaggatcgag ctcttccaga tccttcggcc
      781 agatgagcac attgccaaac agcgctatat cggtggcaag aatctgccca cacggggcac
      841 tgccgagtgg ctgtcctttg atgtcactga cactgtgcgt gagtggctgt tgagaagaga
      901 gtccaactta ggtctagaaa tcagcattca ctgtccatgt cacacctttc agcccaatgg
      961 agatatcctg gaaaacattc acgaggtgat ggaaatcaaa ttcaaaggcg tggacaatga
     1021 ggatgaccat ggccgtggag atctggggcg cctcaagaag cagaaggatc accacaaccc
     1081 tcatctaatc ctcatgatga ttcccccaca ccggctcgac aacccgggcc aggggggtca
     1141 gaggaagaag cgggctttgg acaccaatta ctgcttccgc aacttggagg agaactgctg
     1201 tgtgcgcccc ctctacattg acttccgaca ggatctgggc tggaagtggg tccatgaacc
     1261 taagggctac tatgccaact tctgctcagg cccttgccca tacctccgca gtgcagacac
     1321 aacccacagc acggtgctgg gactgtacaa cactctgaac cctgaagcat ctgcctcgcc
     1381 ttgctgcgtg ccccaggacc tggagcccct gaccatcctg tactatgttg ggaggacccc
     1441 caaagtggag cagctctcca acatggtggt gaagtcttgt aaatgtagct gagaccccac
     1501 gtgcgacaga gagaggggag agagaaccac cactgcctga ctgcccgctc ctcgggaaac
     1561 acacaagcaa caaacctcac tgagaggcct ggagcccaca accttcggct ccgggcaaat
     1621 ggctgagatg gaggtttcct tttggaacat ttctttcttg ctggctctga gaatcacggt
     1681 ggtaaagaaa gtgtgggttt ggttagagga aggctgaact cttcagaaca cacagacttt
     1741 ctgtgacgca gacagagggg atggggatag aggaaaggga tggtaagttg agatgttgtg
     1801 tggcaatggg atttgggcta ccctaaaggg agaaggaagg gcagagaatg gctgggtcag
     1861 ggccagactg gaagacactt cagatctgag gttggatttg ctcattgctg taccacatct
     1921 gctctaggga atctggatta tgttatacaa ggcaagcatt ttttttttta aagacaggtt
     1981 acgaagacaa agtcccagaa ttgtatctca tactgtctgg gattaagggc aaatctatta
     2041 cttttgcaaa ctgtcctcta catcaattaa catcgtgggt cactacaggg agaaaatcca
     2101 ggtcatgcag ttcctggccc atcaactgta ttgggccttt tggatatgct gaacgcagaa
     2161 gaaagggtgg aaatcaaccc tctcctgtct gccctctggg tccctcctct cacctctccc
     2221 tcgatcatat ttccccttgg acacttggtt agacgccttc caggtcagga tgcacatttc
     2281 tggattgtgg ttccatgcag ccttggggca ttatgggtct tcccccactt cccctccaag
     2341 accctgtgtt catttggtgt tcctggaagc aggtgctaca acatgtgagg cattcgggga
     2401 agctgcacat gtgccacaca gtgacttggc cccagacgca tagactgagg tataaagaca
     2461 agtatgaata ttactctcaa aatctttgta taaataaata tttttggggc atcctggatg
     2521 atttcatctt ctggaatatt gtttctagaa cagtaaaagc cttattctaa ggtg
//
```

FIG. 2

```
LOCUS       HSU22431     3678 bp    mRNA            PRI       28-JUN-1995
DEFINITION  Human hypoxia-inducible factor 1 alpha (HIF-1 alpha) mRNA, complete
            cds.
ACCESSION   U22431
NID         g881345
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 3678)
  AUTHORS   Wang,G.L., Jiang,B.H., Rue,E.A. and Semenza,G.L.
  TITLE     Hypoxia-inducible factor 1 is a basic-helix-loop-helix-PAS
            heterodimer regulated by cellular O2 tension
  JOURNAL   Proc. Natl. Acad. Sci. U.S.A. 92 (12), 5510-5514 (1995)
  MEDLINE   95296340
REFERENCE   2  (bases 1 to 3678)
  AUTHORS   Wang,G.L., Jiang,B.-H., Rue,E.A. and Semenza,G.L.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-MAR-1995) Gregg L. Semenza, Center for Medical
            Genetics, The Johns Hopkins University School of Medicine, 600 N.
            Wolfe St., Baltimore, MD 21287-3914, USA
FEATURES             Location/Qualifiers
     source          1..3678
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
                     /cell_line="Hep3B"
                     /cell_type="hepatoblastoma"
     gene            29..2509
                     /gene="HIF-1 alpha"
     CDS             29..2509
                     /gene="HIF-1 alpha"
                     /standard_name="hypoxia-inducible factor 1, alpha subunit"
                     /note="basic helix-loop-helix transcription factor"
                     /codon_start=1
                     /product="hypoxia-inducible factor 1 alpha"
                     /db_xref="PID:g881346"
                     /translation="MEGAGGANDKKKISSERRKEKSRDAARSRRSKESEVFYELAHQL
                     PLPHNVSSHLDKASVMRLTISYLRVRKLLDAGDLDIEDDMKAQMNCFYLKALDGFVMV
                     LTDDGDMIYISDNVNKYMGLTQFELTGHSVFDFTHPCDHEEMREMLTHRNGLVKKGKE
                     QNTQRSFFLRMKCTLTSRGRTMNIKSATWKVLHCTGHIHVYDTNSNQPQCGYKKPPMT
                     CLVLICEPIPHPSNIEIPLDSKTFLSRHSLDMKFSYCDERITELMGYEPEELLGRSIY
                     EYYHALDSDHLTKTHHDMFTKGQVTTGQYRMLAKRGGYVWVETQATVIYNTKNSQPQC
                     IVCVNYVVSGIIQHDLIFSLQQTECVLKPVESSDMKMTQLFTKVESEDTSSLFDKLKK
                     EPDALTLLAPAAGDTIISLDFGSNDTETDDQQLEEVPLYNDVMLPSPNEKLQNINLAM
                     SPLPTAETPKPLRSSADPALNQEVALKLEPNPESLELSFTMPQIQDQTPSPSDGSTRQ
                     SSPEPNSPSEYCFYVDSDMVNEFKLELVEKLFAEDTEAKNPFSTQDTDLDLEMLAPYI
                     PMDDDFQLRSFDQLSPLESSSASPESASPQSTVTVFQQTQIQEPTANATTTTATTDEL
                     KTVTKDRMEDIKILIASPSPTHIHKETTSATSSPYRDTQSRTASPNRAGKGVIEQTEK
                     SHPRSPNVLSVALSQRTTVPEEELNPKILALQNAQRKRKMEHDGSLFQAVGIGTLLQQ
                     PDDHAATTSLSWKRVKGCKSSEQNGMEQKTIILIPSDLACRLLGQSMDESGLPQLTSY
                     DCEVNAPIQGSRNLLQGEELLRALDQVN"
     polyA_site      3678
                     /note="42 A nucleotides"
BASE COUNT     1197 a    695 c    675 g    1111 t
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FIG. 2 (cont'd)

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ORIGIN
        1 gtgaagacat cgcggggacc gattcaccat ggagggcgcc ggcggcgcga acgacaagaa
       61 aaagataagt tctgaacgtc gaaaagaaaa gtctcgagat gcagccagat ctcggcgaag
      121 taaagaatct gaagtttttt atgagcttgc tcatcagttg ccacttccac ataatgtgag
      181 ttcgcatctt gataaggcct ctgtgatgag gcttaccatc agctatttgc gtgtgaggaa
      241 acttctggat gctggtgatt tggatattga agatgacatg aaagcacaga tgaattgctt
      301 ttatttgaaa gccttggatg gttttgttat ggttctcaca gatgatggtg acatgattta
      361 catttctgat aatgtgaaca aatacatggg attaactcag tttgaactaa ctggacacag
      421 tgtgtttgat tttactcatc catgtgacca tgaggaaatg agagaaatgc ttacacacag
      481 aaatggcctt gtgaaaaagg gtaaagaaca aaacacacag cgaagctttt ttctcagaat
      541 gaagtgtacc ctaactagcc gaggaagaac tatgaacata aagtctgcaa catggaaggt
      601 attgcactgc acaggccaca ttcacgtata tgataccaac agtaaccaac ctcagtgtgg
      661 gtataagaaa ccacctatga cctgcttggt gctgatttgt gaacccattc ctcacccatc
      721 aaatattgaa attcctttag atagcaagac tttcctcagt cgacacagcc tggatatgaa
      781 attttcttat tgtgatgaaa gaattaccga attgatggga tatgagccag aagaactttt
      841 aggccgctca atttatgaat attatcatgc tttggactct gatcatctga ccaaaactca
      901 tcatgatatg tttactaaag gacaagtcac cacaggacag tacaggatgc ttgccaaaag
      961 aggtggatat gtctgggttg aaactcaagc aactgtcata tataacacca agaattctca
     1021 accacagtgc attgtatgtg tgaattacgt tgtgagtggt attattcagc acgacttgat
     1081 tttctccctt caacaaacag aatgtgtcct taaaccggtt gaatcttcag atatgaaaat
     1141 gactcagcta ttcaccaaag ttgaatcaga agatacaagt agcctctttg acaaacttaa
     1201 gaaggaacct gatgctttaa ctttgctggc cccagccgct ggagacacaa tcatatcttt
     1261 agattttggc agcaacgaca cagaaactga tgaccagcaa cttgaggaag taccattata
     1321 taatgatgta atgctcccct cacccaacga aaaattacag aatataaatt tggcaatgtc
     1381 tccattaccc accgctgaaa cgccaaagcc acttcgaagt agtgctgacc ctgcactcaa
     1441 tcaagaagtt gcattaaaat tagaaccaaa tccagagtca ctggaacttt cttttaccat
     1501 gccccagatt caggatcaga cacctagtcc ttccgatgga agcactagac aaagttcacc
     1561 tgagcctaat agtcccagtg aatattgttt ttatgtggat agtgatatgg tcaatgaatt
     1621 caagttggaa ttggtagaaa aactttttgc tgaagacaca gaagcaaaga acccattttc
     1681 tactcaggac acagatttag acttggagat gttagctccc tatatcccaa tggatgatga
     1741 cttccagtta cgttccttcg atcagttgtc accattagaa agcagttccg caagccctga
     1801 aagcgcaagt cctcaaagca cagttacagt attccagcag actcaaatac aagaacctac
     1861 tgctaatgcc accactacca ctgccaccac tgatgaatta aaaacagtga caaaagaccg
     1921 tatggaagac attaaaatat tgattgcatc tccatctcct acccacatac ataaagaaac
     1981 tactagtgcc acatcatcac catatagaga tactcaaagt cggacagcct caccaaacag
     2041 agcaggaaaa ggagtcatag aacagacaga aaaatctcat ccaagaagcc ctaacgtgtt
     2101 atctgtcgct ttgagtcaaa gaactacagt tcctgaggaa gaactaaatc caaagatact
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     2221 agtaggaatt ggaacattat tacagcagcc agacgatcat gcagctacta catcactttc
     2281 ttggaaacgt gtaaaaggat gcaaatctag tgaacagaat ggaatggagc aaaagacaat
     2341 tattttaata ccctctgatt tagcatgtag actgctgggg caatcaatgg atgaaagtgg
     2401 attaccacag ctgaccagtt atgattgtga agttaatgct cctatacaag gcagcagaaa
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     2521 atttcattcc tttttttgga cactggtggc tcactaccta aagcagtcta tttatatttt
     2581 ctacatctaa ttttagaagc ctggctacaa tactgcacaa acttggttag ttcaattttt
     2641 gatccccttt ctacttaatt tacattaatg ctctttttta gtatgttctt taatgctgga
     2701 tcacagacag ctcattttct cagtttttg gtatttaaac cattgcattg cagtagcatc
     2761 attttaaaaa atgcaccttt ttatttattt atttttggct agggagttta tccctttttc
     2821 gaattatttt taagaagatg ccaatataat tttgtaaga aggcagtaac ctttcatcat
     2881 gatcataggc agttgaaaaa tttttacacc tttttttca cattttacat aaataataat
     2941 gctttgccag cagtacgtgg tagccacaat tgcacaatat attttcttaa aaaataccag
     3001 cagttactca tggaatatat tctgcgttta taaaactagt ttttaagaag aaattttttt
     3061 tggcctatga aattgttaaa cctggaacat gacattgtta atcatataat aatgattctt
     3121 aaatgctgta tggtttatta tttaaatggg taaagccatt tacataatat agaaagatat
     3181 gcatatatct agaaggtatg tggcatttat ttggataaaa ttctcaattc agagaaatca
     3241 tctgatgttt ctatagtcac tttgccagct caaaagaaaa caatacccta tgtagttgtg
     3301 gaagtttatg ctaatattgt gtaactgata ttaaacctaa atgttctgcc taccctgttg
     3361 gtataaagat attttgagca gactgtaaac aagaaaaaaa aaatcatgca ttcttagcaa
     3421 aattgcctag tatgttaatt tgctcaaaat acaatgtttg attttatgca ctttgtcgct
     3481 attaacatcc ttttttcat gtagatttca ataattgagt aattttagaa gcattatttt
     3541 aggaatatat agttgtcaca gtaaatatct tgtttttct atgtacattg tacaaatttt
     3601 tcattccttt tgctctttgt ggttggatct aacactaact gtattgtttt gttacatcaa
     3661 ataaacatct tctgtgga
```

FIG. 3A

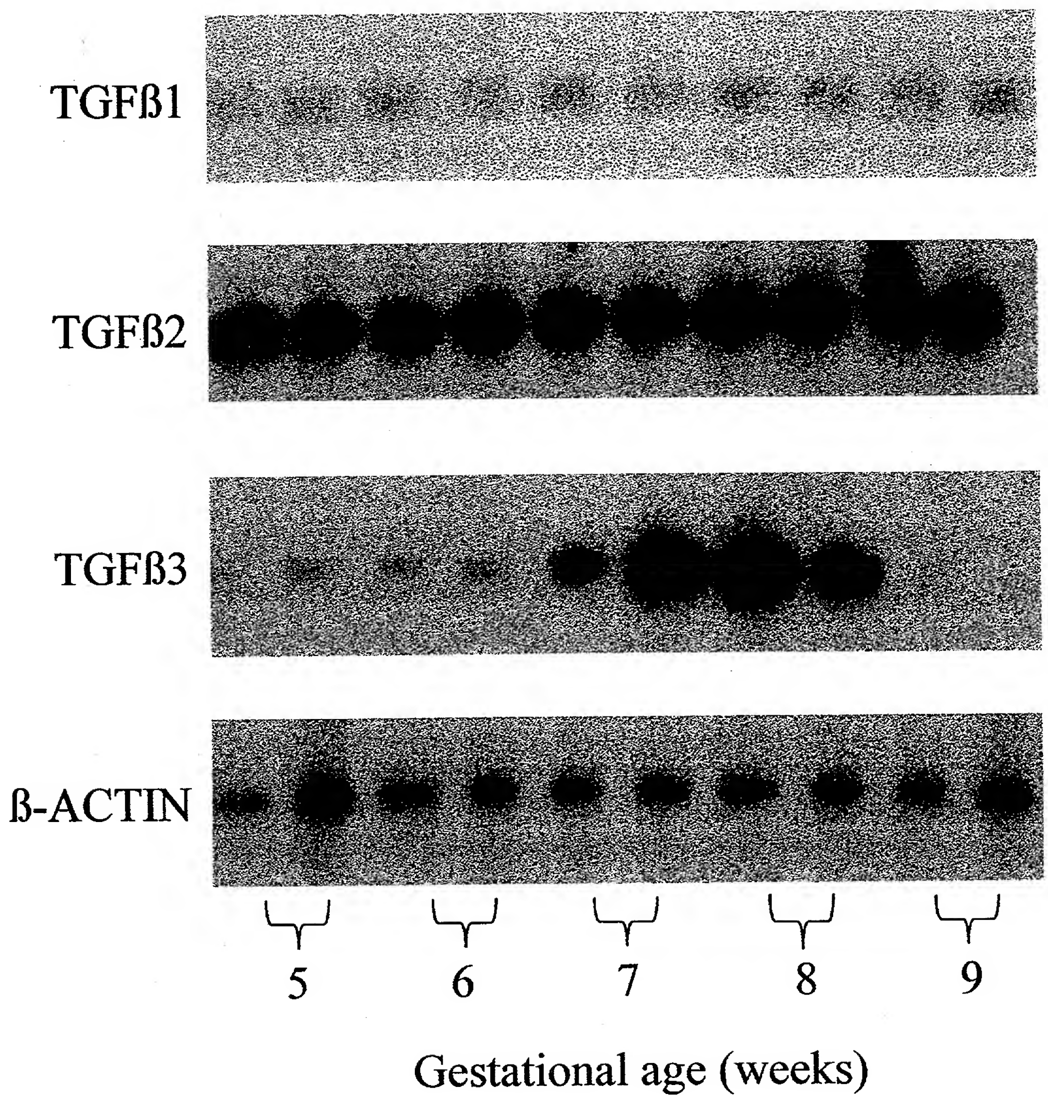
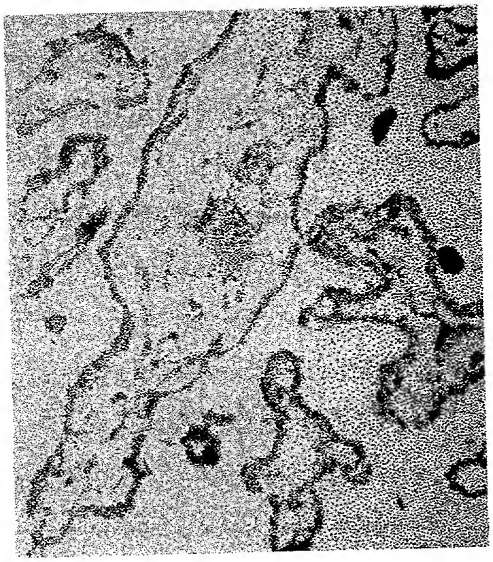
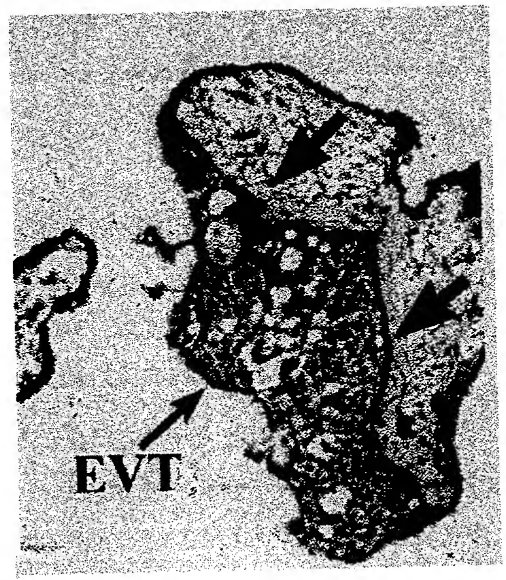


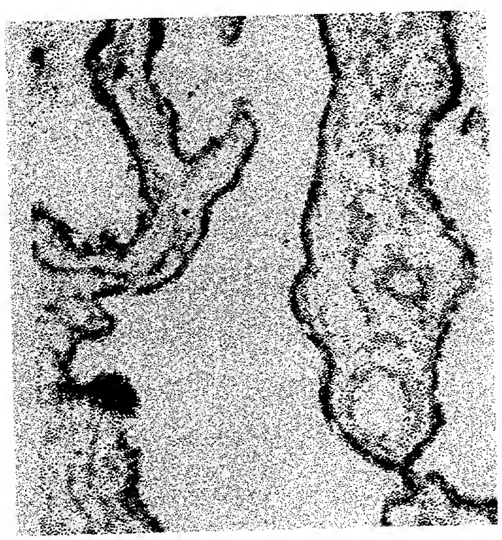
FIG. 3B



5 weeks



8 weeks



12 weeks

8 weeks (control)

FIG. 4A

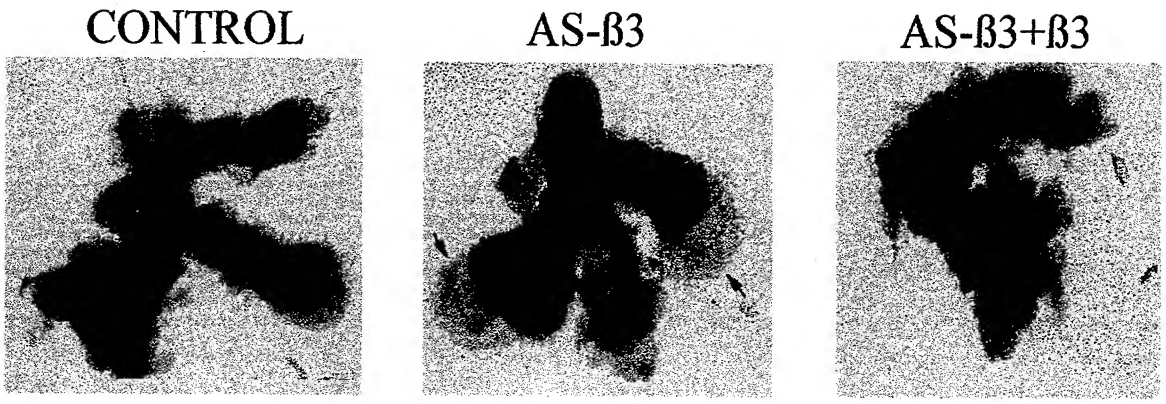


FIG. 4B

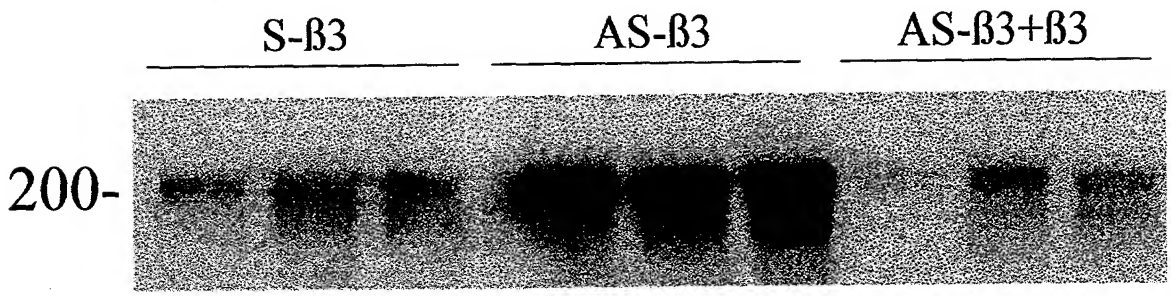


FIG. 4C

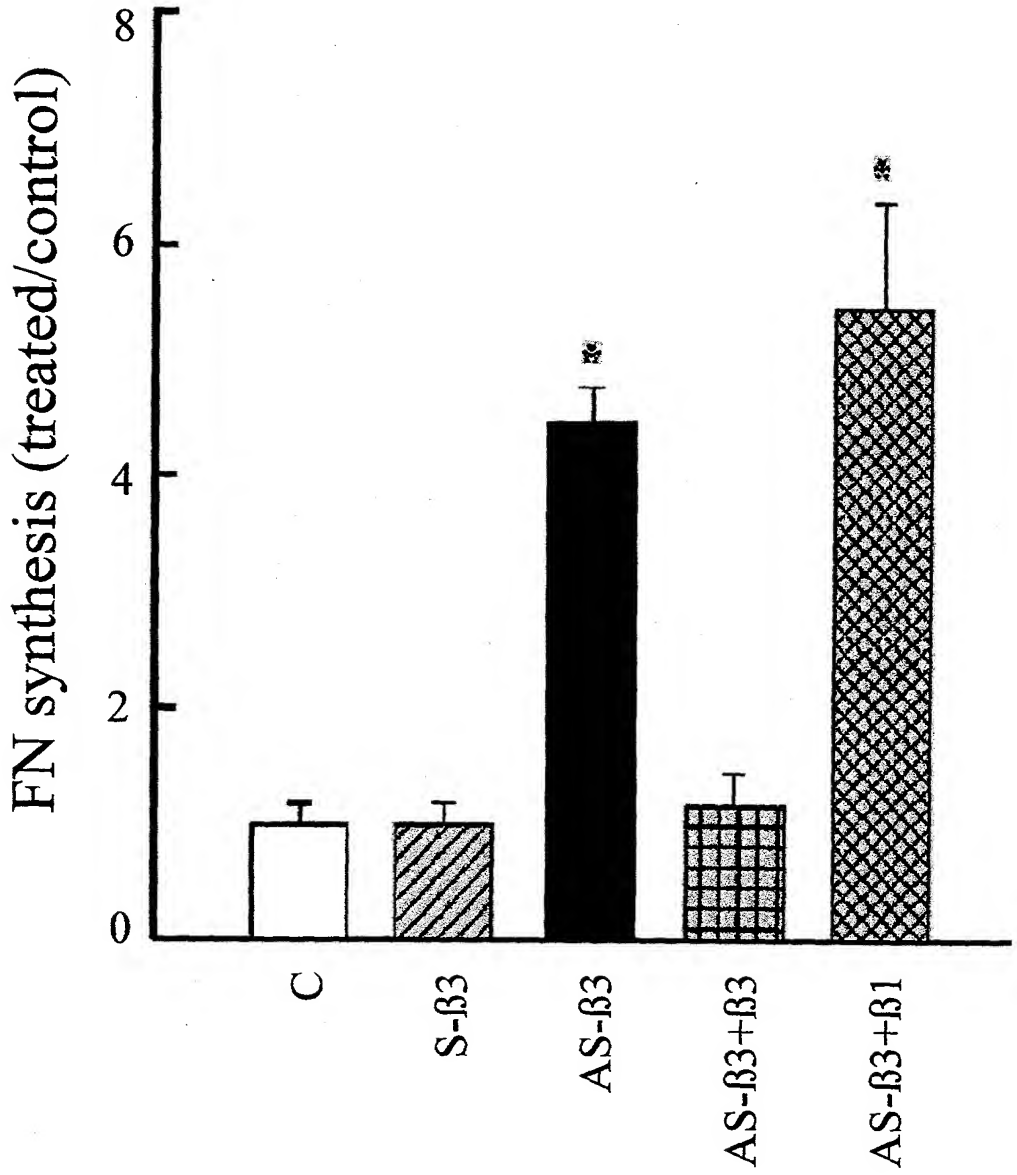

FN synthesis (treated/control)
8
6
4
2
0
C
S-β3
AS-β3
AS-β3+β3
AS-β3+β1

FIG. 4D

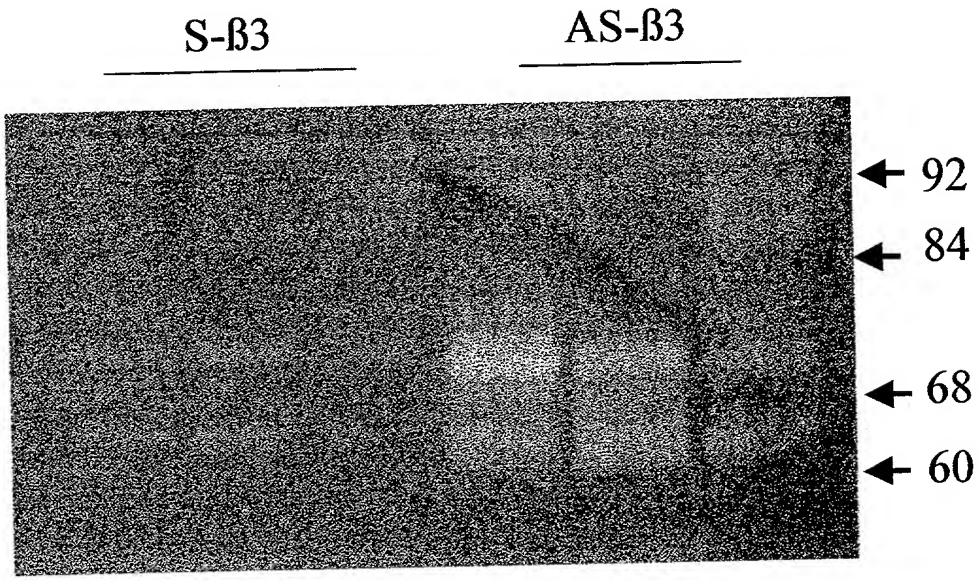


FIG. 4E

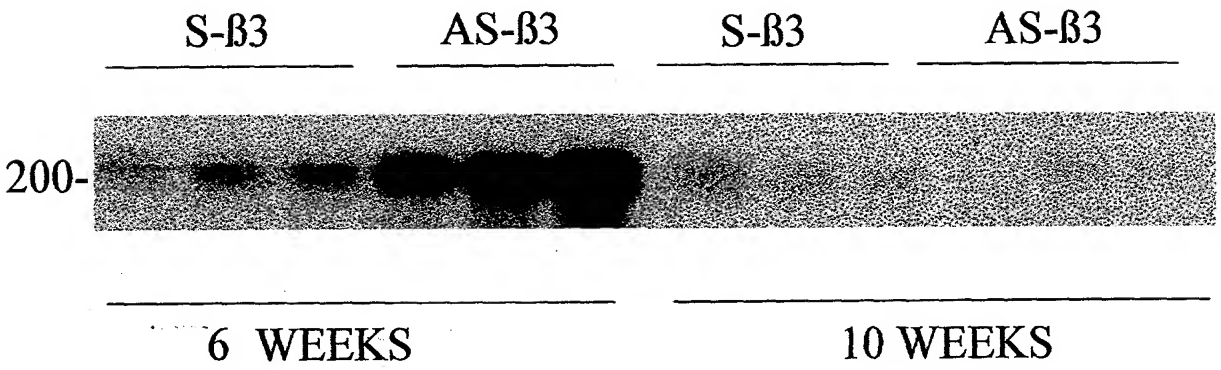


FIG. 5A

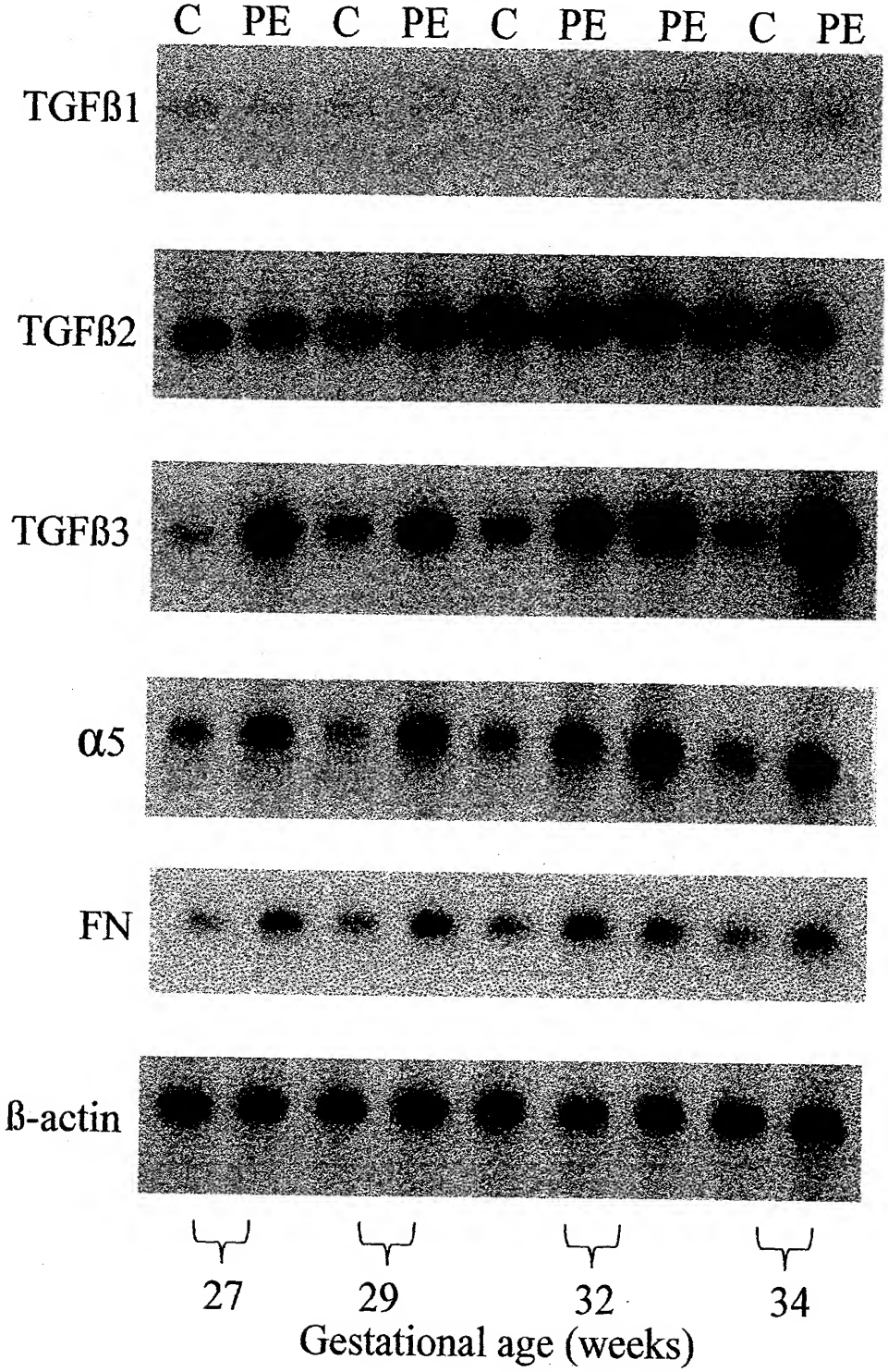

C PE C PE C PE PE C PE
TGFß1
TGFß2
TGFß3
α5
FN
ß-actin
27
29
32
34
Gestational age (weeks)

FIG. 5B

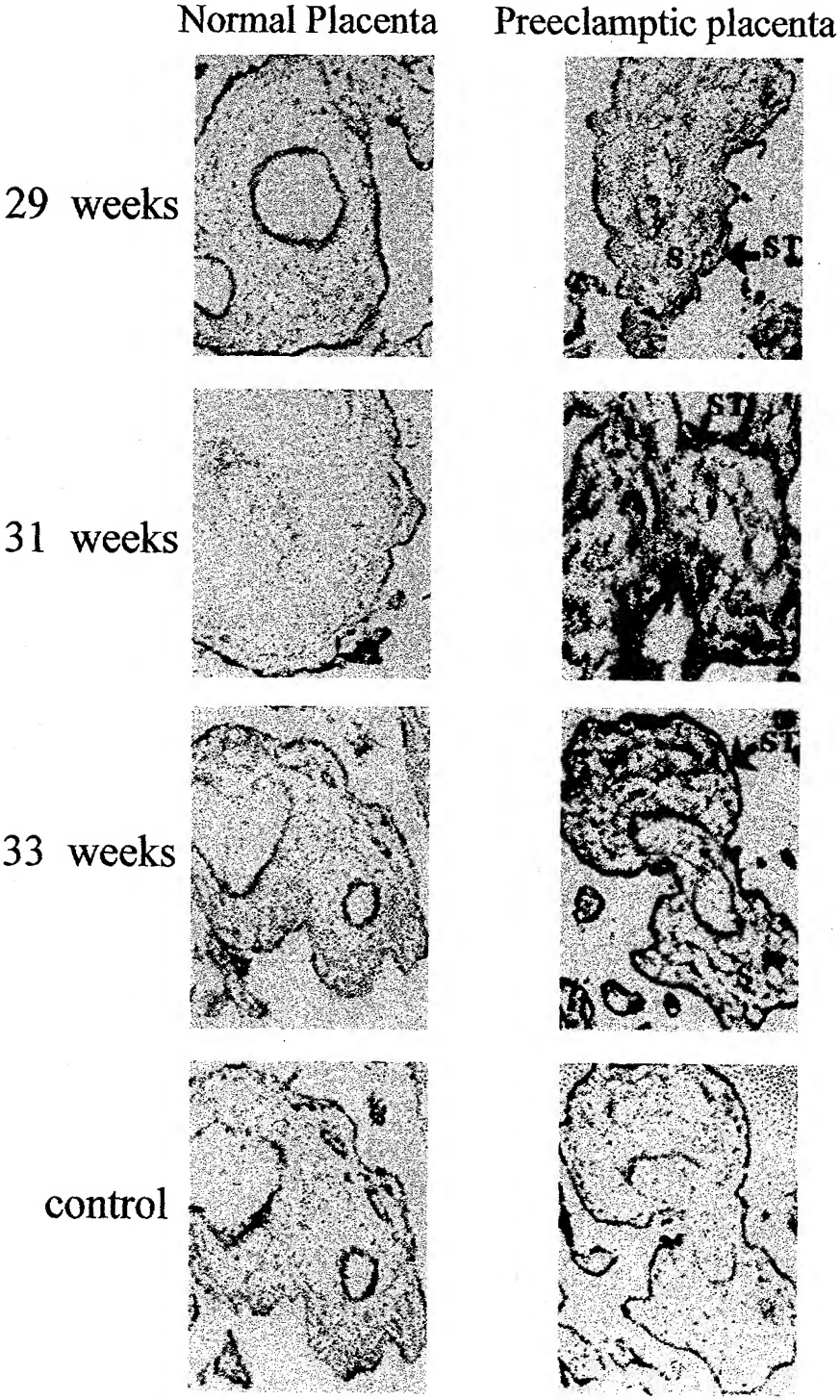
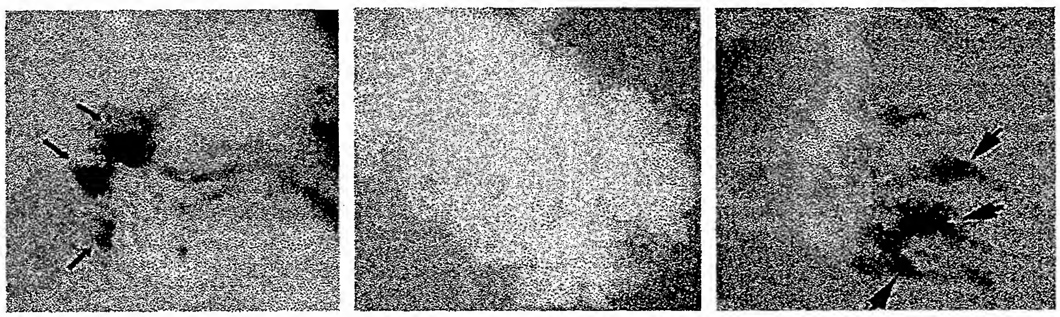


FIG. 6A

Normal Placenta Preeclamptic placenta



S-ß3 S-ß3 AS-ß3

FIG. 6B

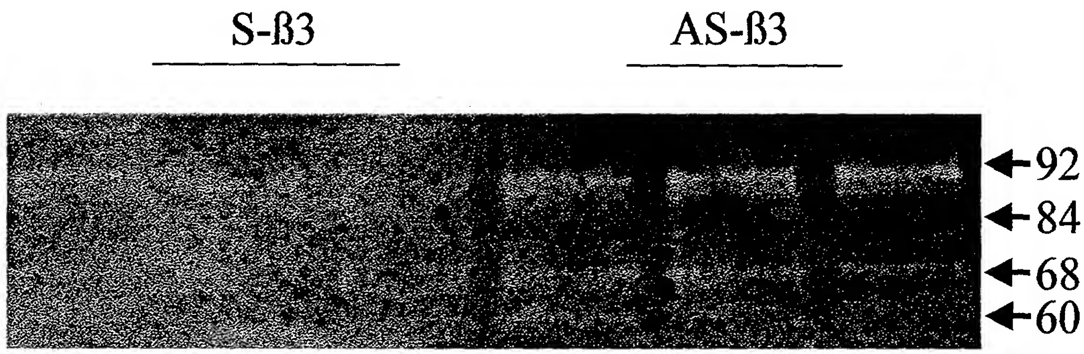


FIG. 6C

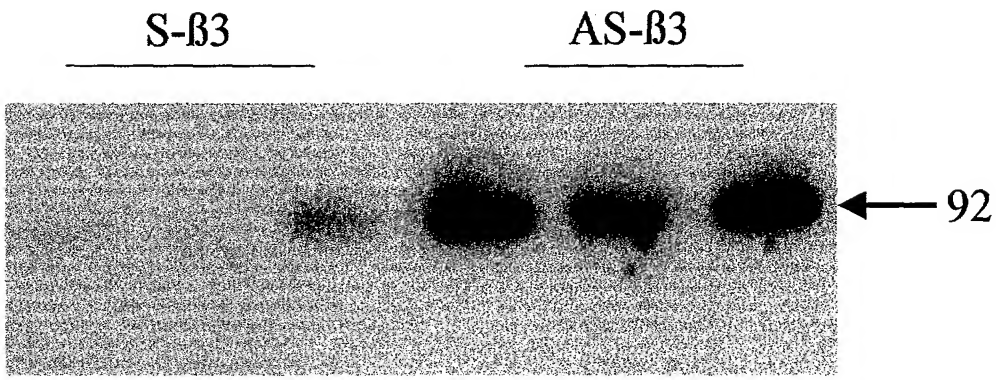


FIG. 7A

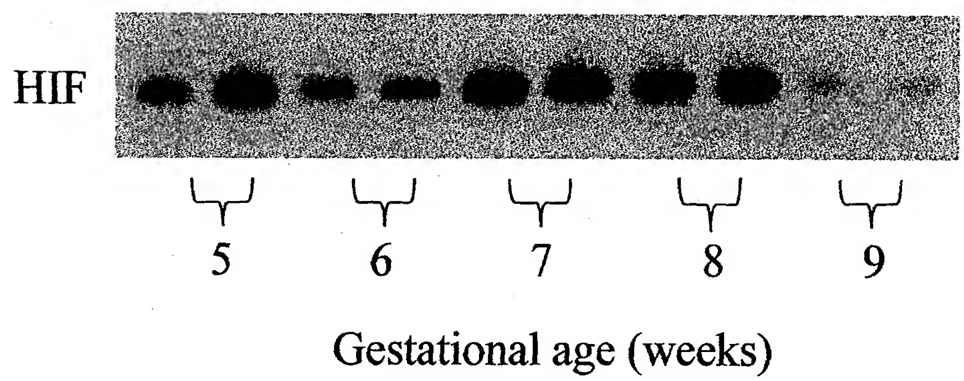


FIG. 7B

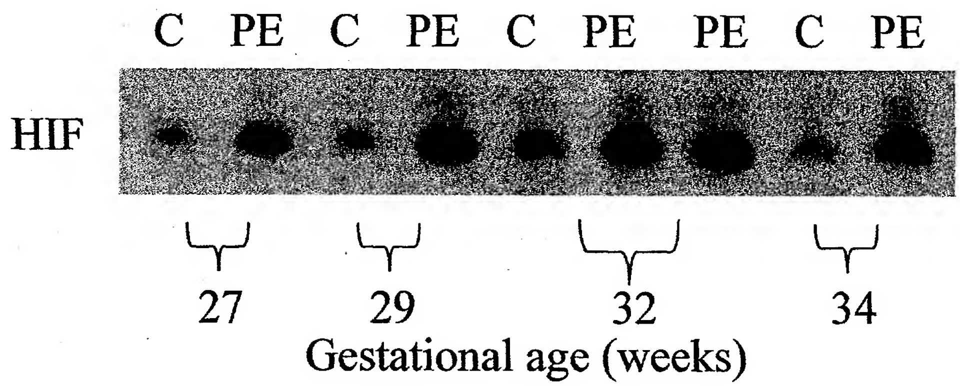


FIG. 8

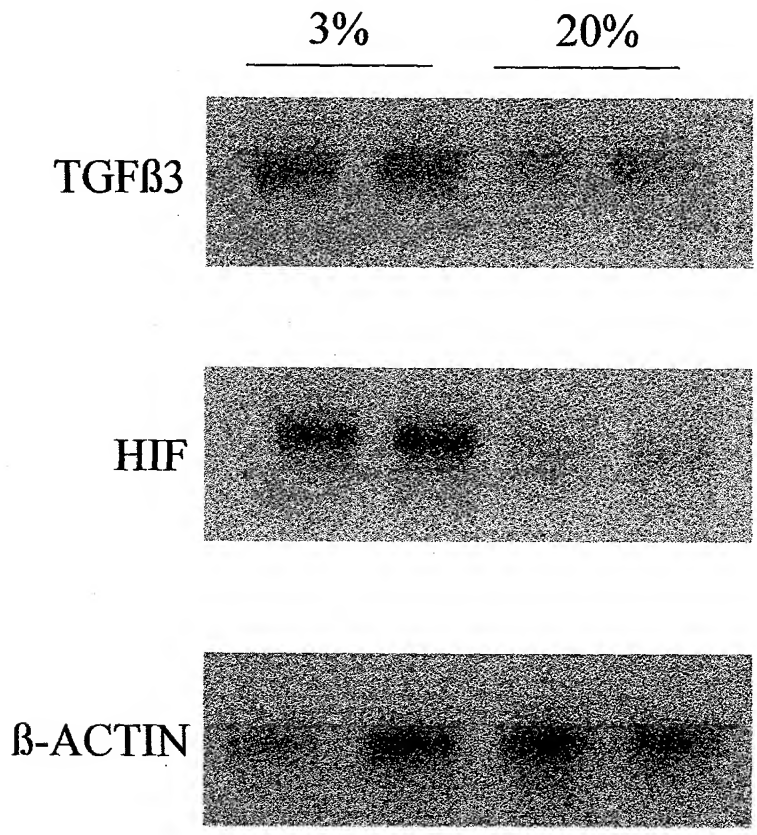


FIG. 9

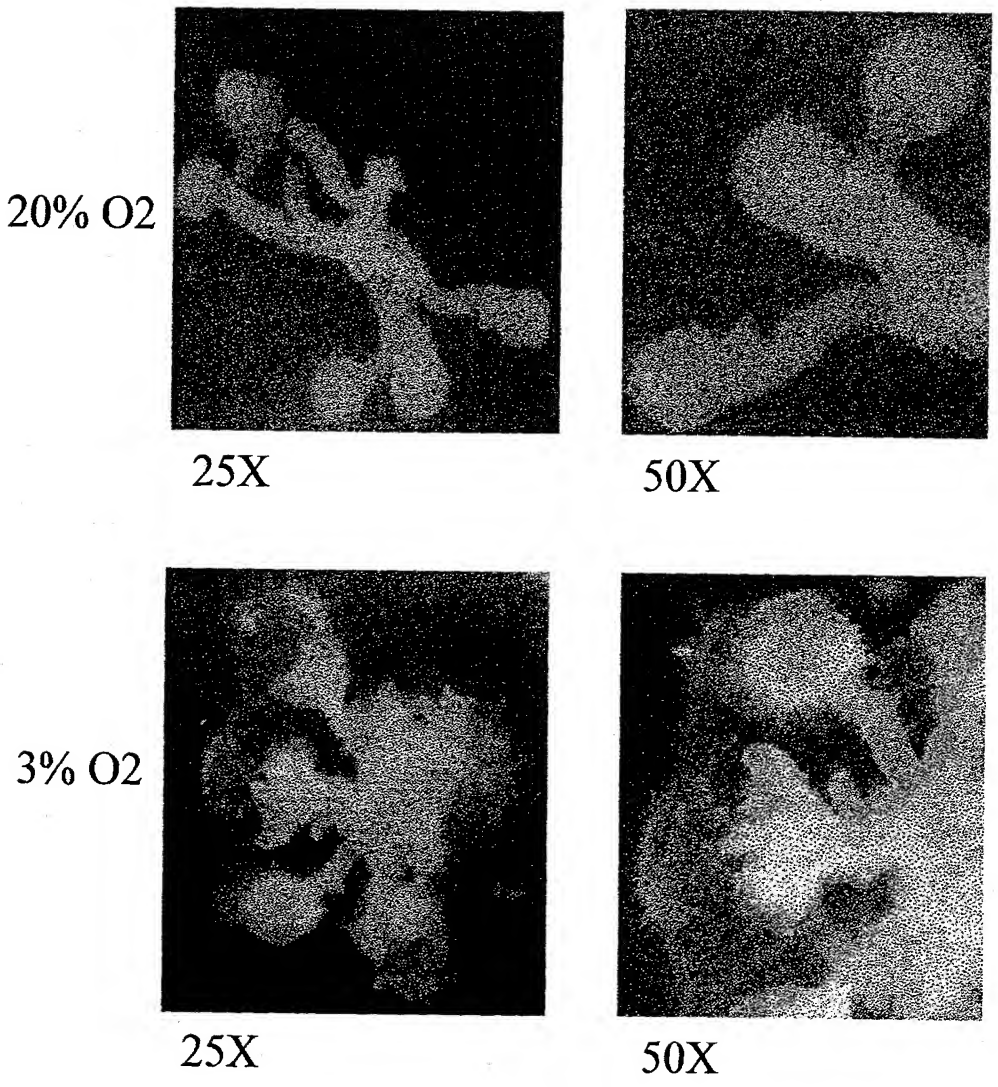


FIG. 10